General

Guideline Title

Ectopic pregnancy and miscarriage: diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage.

Bibliographic Source(s)

National Collaborating Centre for Women's and Children's Health. Ectopic pregnancy and miscarriage. Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Dec. 38 p. (Clinical guideline; no. 154).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Women's and Children's Health on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Terms Used in this Guideline

Early pregnancy: Pregnancy in the first trimester – that is, up to 13 completed weeks of pregnancy.

Expectant management: A management approach in which treatment is not administered, with the aim of seeing whether the condition will resolve naturally.

Pregnancy of unknown location: A descriptive term used to classify a pregnancy when a woman has a positive pregnancy test but no pregnancy can be seen on an ultrasound scan.

Support and Information Giving

Treat all women with *early pregnancy* complications with dignity and respect. Be aware that women will react to complications or the loss of a pregnancy in different ways. Provide all women with information and support in a sensitive manner, taking into account their individual circumstances and emotional response.[1]

Healthcare professionals providing care for women with early pregnancy complications in any setting should be aware that early pregnancy complications can cause significant distress for some women and their partners. Healthcare professionals providing care for these women should be given training in how to communicate sensitively and breaking bad news. Nonclinical staff such as receptionists working in settings where early

pregnancy care is provided should also be given training on how to communicate sensitively with women who experience early pregnancy complications.

Throughout a woman's care, give her and (with agreement) her partner specific evidence-based information in a variety of formats. This should include (as appropriate):

- When and how to seek help if existing symptoms worsen or new symptoms develop, including a 24-hour contact telephone number.
- What to expect during the time she is waiting for an ultrasound scan.
- What to expect during the course of her care (including expectant management), such as the potential length and extent of pain and/or bleeding, and possible side effects. This information should be tailored to the care she receives.
- Information about post-operative care (for women undergoing surgery).
- What to expect during the recovery period – for example, when it is possible to resume sexual activity and/or try to conceive again, and what to do if she becomes pregnant again. This information should be tailored to the care she receives.
- Information about the likely impact of her treatment on future fertility.
- Where to access support and counselling services, including leaflets, web addresses and helpline numbers for support organisations.

Ensure that sufficient time is available to discuss these issues with women during the course of their care and arrange an additional appointment if more time is needed.

After an early pregnancy loss, offer the woman the option of a follow-up appointment with a healthcare professional of her choice.

Early Pregnancy Assessment Services

Regional services should be organised so that an early pregnancy assessment service is available 7 days a week for women with early pregnancy complications, where scanning can be carried out and decisions about management made.

An early pregnancy assessment service should:

- Be a dedicated service provided by healthcare professionals competent to diagnose and care for women with pain and/or bleeding in early pregnancy and
- Offer ultrasound and assessment of serum human chorionic gonadotrophin (hCG) levels and
- Be staffed by healthcare professionals with training in sensitive communication and breaking bad news

Early pregnancy assessment services should accept self-referrals from women who have had recurrent miscarriage[2] or a previous ectopic or molar pregnancy. All other women with pain and/or bleeding should be assessed by a healthcare professional (such as a general practitioner [GP], accident and emergency [A&E] doctor, midwife or nurse) before referral to an early pregnancy assessment service.

Ensure that a system is in place to enable women referred to their local early pregnancy assessment service to attend within 24 hours if the clinical situation warrants this. If the service is not available, and the clinical symptoms warrant further assessment, refer women to the nearest accessible facility that offers specialist clinical assessment and ultrasound scanning (such as a gynaecology ward or A&E service with access to specialist gynaecology support).

Symptoms and Signs of Ectopic Pregnancy and Initial Assessment

Refer women who are haemodynamically unstable, or in whom there is significant concern about the degree of pain or bleeding, directly to A&E.

Be aware that atypical presentation for ectopic pregnancy is common.

Be aware that ectopic pregnancy can present with a variety of symptoms. Even if a symptom is less common, it may still be significant. Symptoms of ectopic pregnancy include:

- Common symptoms:
  - Abdominal or pelvic pain
  - Amenorrhoea or missed period
  - Vaginal bleeding with or without clots
- Other reported symptoms:
  - Breast tenderness
  - Gastrointestinal symptoms
  - Dizziness, fainting or syncope

    - Shoulder tip pain
    - Urinary symptoms
    - Passage of tissue
    - Rectal pressure or pain on defecation

Be aware that ectopic pregnancy can present with a variety of signs on examination by a healthcare professional. Signs of ectopic pregnancy include:

- More common signs:
    - Pelvic tenderness
    - Adnexal tenderness
    - Abdominal tenderness
- Other reported signs:
    - Cervical motion tenderness
    - Rebound tenderness or peritoneal signs
    - Pallor
    - Abdominal distension
    - Enlarged uterus
    - Tachycardia (more than 100 beats per minute) or hypotension (less than 100/60 mmHg)
    - Shock or collapse
    - Orthostatic hypotension

During clinical assessment of women of reproductive age, be aware that:

- They may be pregnant, and think about offering a pregnancy test even when symptoms are non-specific and
- The symptoms and signs of ectopic pregnancy can resemble the common symptoms and signs of other conditions – for example, gastrointestinal conditions or urinary tract infection

All healthcare professionals involved in the care of women of reproductive age should have access to pregnancy tests.

Refer immediately to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) for further assessment women with a positive pregnancy test and the following on examination:

- Pain and abdominal tenderness or
- Pelvic tenderness or
- Cervical motion tenderness

Exclude the possibility of ectopic pregnancy, even in the absence of risk factors (such as previous ectopic pregnancy), because about a third of women with an ectopic pregnancy will have no known risk factors.

Refer to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) women with bleeding or other symptoms and signs of early pregnancy complications who have:

- Pain or
- A pregnancy of 6 weeks gestation or more or
- A pregnancy of uncertain gestation

The urgency of this referral depends on the clinical situation.

Use expectant management for women with a pregnancy of less than 6 weeks gestation who are bleeding but not in pain. Advise these women:

- To repeat a urine pregnancy test after 7–10 days and to return if it is positive
- A negative pregnancy test means that the pregnancy has miscarried
- To return if their symptoms continue or worsen

Refer women who return with worsening symptoms and signs that could suggest an ectopic pregnancy to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) for further assessment. The decision about whether she should be seen immediately or within 24 hours will depend on the clinical situation.

If a woman is referred to an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available), explain the reasons for the referral and what she can expect when she arrives there.

Diagnosis of Viable Intrauterine Pregnancy and of Ectopic Pregnancy

Using Ultrasound for Diagnosis

Offer women who attend an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) a transvaginal ultrasound scan to identify the location of the pregnancy and whether there is a fetal pole and heartbeat.

Consider a transabdominal ultrasound scan for women with an enlarged uterus or other pelvic pathology, such as fibroids or an ovarian cyst.

If a transvaginal ultrasound scan is unacceptable to the woman, offer a transabdominal ultrasound scan and explain the limitations of this method of scanning.

Inform women that the diagnosis of miscarriage using 1 ultrasound scan cannot be guaranteed to be 100% accurate and there is a small chance that the diagnosis may be incorrect, particularly at very early gestational ages.

When performing an ultrasound scan to determine the viability of an intrauterine pregnancy, first look to identify a fetal heartbeat. If there is no visible heartbeat but there is a visible fetal pole, measure the crown-rump length. Only measure the mean gestational sac diameter if the fetal pole is not visible.

If the crown–rump length is less than 7.0 mm with a transvaginal ultrasound scan and there is no visible heartbeat, perform a second scan a minimum of 7 days after the first before making a diagnosis. Further scans may be needed before a diagnosis can be made.

If the crown–rump length is 7.0 mm or more with a transvaginal ultrasound scan and there is no visible heartbeat:

- Seek a second opinion on the viability of the pregnancy and/or
- Perform a second scan a minimum of 7 days after the first before making a diagnosis

If there is no visible heartbeat when the crown–rump length is measured using a transabdominal ultrasound scan:

- Record the size of the crown–rump length and
- Perform a second scan a minimum of 14 days after the first before making a diagnosis

If the mean gestational sac diameter is less than 25.0 mm with a transvaginal ultrasound scan and there is no visible fetal pole, perform a second scan a minimum of 7 days after the first before making a diagnosis. Further scans may be needed before a diagnosis can be made.

If the mean gestational sac diameter is 25.0 mm or more using a transvaginal ultrasound scan and there is no visible fetal pole:

- Seek a second opinion on the viability of the pregnancy and/or
- Perform a second scan a minimum of 7 days after the first before making a diagnosis

If there is no visible fetal pole and the mean gestational sac diameter is measured using a transabdominal ultrasound scan:

- Record the size of the mean gestational sac diameter and
- Perform a second scan a minimum of 14 days after the first before making a diagnosis

Do not use gestational age from the last menstrual period alone to determine whether a fetal heartbeat should be visible.

Inform women that the date of their last menstrual period may not give an accurate representation of gestational age because of variability in the menstrual cycle.

Inform women what to expect while waiting for a repeat scan and that waiting for a repeat scan has no detrimental effects on the outcome of the pregnancy.

Give women a 24-hour contact telephone number so that they can speak to someone with experience of caring for women with early pregnancy complications who understands their needs and can advise on appropriate care.[3]

When diagnosing complete miscarriage on an ultrasound scan, in the absence of a previous scan confirming an intrauterine pregnancy, always be aware of the possibility of ectopic pregnancy. Advise these women to return for further review if their symptoms persist.

All ultrasound scans should be performed and reviewed by someone with training in, and experience of, diagnosing ectopic pregnancies.

Human Chorionic Gonadotrophin Measurements in Women with Pregnancy of Unknown Location

Be aware that women with a *pregnancy of unknown location* could have an ectopic pregnancy until the location is determined.

Do not use serum hCG measurements to determine the location of the pregnancy.

In a woman with a pregnancy of unknown location, place more importance on clinical symptoms than on serum hCG results, and review the woman's condition if any of her symptoms change, regardless of previous results and assessments.

Use serum hCG measurements only for assessing trophoblastic proliferation to help to determine subsequent management.

Take 2 serum hCG measurements as near as possible to 48 hours apart (but no earlier) to determine subsequent management of a pregnancy of unknown location. Take further measurements only after review by a senior healthcare professional.

Regardless of serum hCG levels, give women with a pregnancy of unknown location written information about what to do if they experience any new or worsening symptoms, including details about how to access emergency care 24 hours a day. Advise women to return if there are new symptoms or if existing symptoms worsen.

For a woman with an increase in serum hCG concentration greater than 63% after 48 hours:

- Inform her that she is likely to have a developing intrauterine pregnancy (although the possibility of an ectopic pregnancy cannot be excluded).
- Offer her a transvaginal ultrasound scan to determine the location of the pregnancy between 7 and 14 days later. Consider an earlier scan for women with a serum hCG level greater than or equal to 1500 IU/litre.
    - If a viable intrauterine pregnancy is confirmed, offer her routine antenatal care[4]
    - If a viable intrauterine pregnancy is not confirmed, refer her for immediate clinical review by a senior gynaecologist

For a woman with a decrease in serum hCG concentration greater than 50% after 48 hours:

- Inform her that the pregnancy is unlikely to continue but that this is not confirmed and
- Provide her with oral and written information about where she can access support and counselling services[3] and
- Ask her to take a urine pregnancy test 14 days after the second serum hCG test, and explain that:
    - If the test is negative, no further action is necessary
    - if the test is positive, she should return to the early pregnancy assessment service for clinical review within 24 hours

For a woman with a change in serum hCG concentration between a 50% decline and 63% rise inclusive, refer her for clinical review in the early pregnancy assessment service within 24 hours.

For women with a pregnancy of unknown location, when using serial serum hCG measurements, do not use serum progesterone measurements as an adjunct to diagnose either viable intrauterine pregnancy or ectopic pregnancy.

Management of Miscarriage

Threatened Miscarriage

Advise a woman with vaginal bleeding and a confirmed intrauterine pregnancy with a fetal heartbeat that:

- If her bleeding gets worse, or persists beyond 14 days, she should return for further assessment
- If the bleeding stops, she should start or continue routine antenatal care

Expectant Management

Use expectant management for 7–14 days as the first-line management strategy for women with a confirmed diagnosis of miscarriage. Explore management options other than expectant management if:

- The woman is at increased risk of haemorrhage (for example, she is in the late first trimester) or
- She has previous adverse and/or traumatic experience associated with pregnancy (for example, stillbirth, miscarriage or antepartum haemorrhage) or
- She is at increased risk from the effects of haemorrhage (for example, if she has coagulopathies or is unable to have a blood transfusion) or

- There is evidence of infection

Offer medical management to women with a confirmed diagnosis of miscarriage if expectant management is not acceptable to the woman.

Explain what expectant management involves and that most women will need no further treatment. Also provide women with oral and written information about further treatment options.

Give all women undergoing expectant management of miscarriage oral and written information about what to expect throughout the process, advice on pain relief and where and when to get help in an emergency[3].

If the resolution of bleeding and pain indicate that the miscarriage has completed during 7–14 days of expectant management, advise the woman to take a urine pregnancy test after 3 weeks, and to return for individualised care if it is positive.

Offer a repeat scan if after the period of expectant management the bleeding and pain:

- Have not started (suggesting that the process of miscarriage has not begun) or
- Are persisting and/or increasing (suggesting incomplete miscarriage)

Discuss all treatment options (continued expectant management, medical management, and surgical management) with the woman to allow her to make an informed choice.

Review the condition of a woman who opts for continued expectant management of miscarriage at a minimum of 14 days after the first follow-up appointment.

Medical Management

Do not offer mifepristone as a treatment for missed or incomplete miscarriage.

Offer vaginal misoprostol for the medical treatment of missed or incomplete miscarriage. Oral administration is an acceptable alternative if this is the woman's preference[5].

For women with a missed miscarriage, use a single dose of 800 micrograms of misoprostol[5].

Advise the woman that if bleeding has not started 24 hours after treatment, she should contact her healthcare professional to determine ongoing individualised care.

For women with an incomplete miscarriage, use a single dose of 600 micrograms of misoprostol. (800 micrograms can be used as an alternative to allow alignment of treatment protocols for both missed and incomplete miscarriage[5].)

Offer all women receiving medical management of miscarriage pain relief and anti-emetics as needed.

Inform women undergoing medical management of miscarriage about what to expect throughout the process, including the length and extent of bleeding and the potential side effects of treatment including pain, diarrhoea and vomiting.

Advise women to take a urine pregnancy test 3 weeks after medical management of miscarriage unless they experience worsening symptoms, in which case advise them to return to the healthcare professional responsible for providing their medical management.

Advise women with a positive urine pregnancy test after 3 weeks to return for a review by a healthcare professional to ensure that there is no molar or ectopic pregnancy.

Surgical Management

Where clinically appropriate, offer women undergoing a miscarriage a choice of:

- Manual vacuum aspiration under local anaesthetic in an outpatient or clinic setting or
- Surgical management in a theatre under general anaesthetic

Provide oral and written information to all women undergoing surgical management of miscarriage about the treatment options available and what to expect during and after the procedure[3].

Management of Ectopic Pregnancy

Surgical and Medical Management

Inform women who have had an ectopic pregnancy that they can self-refer to an early pregnancy assessment service in future pregnancies if they have any early concerns.

Give all women with an ectopic pregnancy oral and written information about:

- How they can contact a healthcare professional for post-operative advice if needed, and who this will be and
- Where and when to get help in an emergency[3].

Offer systemic methotrexate[6] as a first-line treatment to women who are able to return for follow-up and who have all of the following:

- No significant pain
- An unruptured ectopic pregnancy with an adnexal mass smaller than 35 mm with no visible heartbeat
- A serum hCG level less than 1500 IU/litre
- No intrauterine pregnancy (as confirmed on an ultrasound scan)

Offer surgery where treatment with methotrexate is not acceptable to the woman.

Offer surgery as a first-line treatment to women who are unable to return for follow-up after methotrexate treatment or who have any of the following:

- An ectopic pregnancy and significant pain
- An ectopic pregnancy with an adnexal mass of 35 mm or larger
- An ectopic pregnancy with a fetal heartbeat visible on an ultrasound scan
- An ectopic pregnancy and a serum hCG level of 5000 IU/litre or more

Offer the choice of either methotrexate[6] or surgical management to women with an ectopic pregnancy who have a serum hCG level of at least 1500 IU/litre and less than 5000 IU/litre, who are able to return for follow-up and who meet all of the following criteria:

- No significant pain
- An unruptured ectopic pregnancy with an adnexal mass smaller than 35 mm with no visible heartbeat
- No intrauterine pregnancy (as confirmed on an ultrasound scan)

Advise women who choose methotrexate that their chance of needing further intervention is increased and they may need to be urgently admitted if their condition deteriorates.

For women with ectopic pregnancy who have had methotrexate, take 2 serum hCG measurements in the first week (days 4 and 7) after treatment and then 1 serum hCG measurement per week until a negative result is obtained. If hCG levels plateau or rise, reassess the woman's condition for further treatment.

Performing Laparoscopy

When surgical treatment is indicated for women with an ectopic pregnancy, it should be performed laparoscopically whenever possible, taking into account the condition of the woman and the complexity of the surgical procedure.

Surgeons providing care to women with ectopic pregnancy should be competent to perform laparoscopic surgery.

Commissioners and managers should ensure that equipment for laparoscopic surgery is available.

Salpingectomy and Salpingotomy

Offer a salpingectomy to women undergoing surgery for an ectopic pregnancy unless they have other risk factors for infertility.

Consider salpingotomy as an alternative to salpingectomy for women with risk factors for infertility such as contralateral tube damage.

Inform women having a salpingotomy that up to 1 in 5 women may need further treatment. This treatment may include methotrexate and/or a salpingectomy.

For women who have had a salpingotomy, take 1 serum hCG measurement at 7 days after surgery, then 1 serum hCG measurement per week until a negative result is obtained.

Advise women who have had a salpingectomy that they should take a urine pregnancy test after 3 weeks. Advise women to return for further assessment if the test is positive.

Anti-D Rhesus Prophylaxis

Offer anti-D rhesus prophylaxis at a dose of 250 IU (50 micrograms) to all rhesus negative women who have a surgical procedure to manage an ectopic pregnancy or a miscarriage.

Do not offer anti-D rhesus prophylaxis to women who:

- Receive solely medical management for an ectopic pregnancy or miscarriage or
- Have a threatened miscarriage or
- Have a complete miscarriage or
- Have a pregnancy of unknown location

Do not use a Kleihauer test for quantifying feto–maternal haemorrhage.

[1] For further guidance about providing information, see Patient experience in adult National Health Service (NHS) services (NICE clinical guidance 138).

[2] Although additional care for women with recurrent miscarriage is not included in the scope of the guideline, the Guideline Development Group recognised that it is common clinical practice to allow these women to self-refer to an early pregnancy assessment service and wished this to remain the case.

[3] See Recommendations above in "Support and Information Giving" for details of further information that should be provided.

[4] See the NICE guideline, Antenatal Care. Routine care for the healthy pregnant woman (NICE Guideline 62).

[5] Although this use is common in UK clinical practice, at the time of publication (December 2012), misoprostol did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors for further information.

[6] Although this use is common in UK clinical practice, at the time of publication (December 2012), methotrexate did not have UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing medicines - guidance for doctors for further information.

Clinical Algorithm(s)

The full version of the original guideline document includes the following care pathways:

- Initial Clinical Assessment
- Initial Ultrasound Scan
- Pregnancy of Unknown Location (PUL)
- Intrauterine Pregnancy
- Management of Miscarriage
- Medical Management of Miscarriage
- Ectopic Pregnancy

In addition, a NICE pathway for ectopic pregnancy and miscarriage is available from the National Institute for Health and Clinical Excellence (NICE) Web site.

Scope

Disease/Condition(s)

- Ectopic pregnancy
- Miscarriage

Note: The guideline does not cover the emergency management of acute presentations of shock and collapse; management of other problems in the first trimester unrelated to pain and bleeding caused by miscarriage or ectopic pregnancy; ongoing management of the pregnancy after the first trimester (that is, 13 completed weeks or more); and additional treatment and care needed by women with recurrent miscarriage.

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Internal Medicine

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Nurses

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Guideline Objective(s)

- To offer best practice advice on the care of women with early pregnancy complications
- To cover diagnosis of early pregnancy loss, including the use of ultrasound scanning and biochemical testing

Target Population

Women in early pregnancy with signs and symptoms of ectopic pregnancy

Interventions and Practices Considered

1. Patient information on course of care and support services
2. Early pregnancy assessment services
3. Assessment of ectopic pregnancy signs and symptoms
4. Transvaginal ultrasound, identifying:
    - Location of pregnancy
    - Fetal pole and heartbeat
5. Consider the pregnancy to be ectopic until location is determined
6. Expectant management for 7-14 days
7. Explore other management if:
    - Increased risk of haemorrhage (in late trimester)
    - Previous adverse effects and/or traumatic experience associated with pregnancy
    - Increased risk from the effects of haemorrhage

    - Evidence of infection
8. Surgical management for miscarriage, including vacuum aspiration
9. Laparoscopy
10. Salpingectomy and salpingotomy

Major Outcomes Considered

- Positive pregnancy test
- Pain and/or bleeding
- Risk of haemorrhage
- Previous adverse or traumatic birth experience
- Evidence of infection
- Risk of infertility

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Women's and Children's Health (NCC-WCH), on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing Review Questions and Protocols and Identifying Evidence

The Guideline Development Group (GDG) formulated review questions based on the scope (see Appendix A of the full version of the original guideline document) and prepared a protocol for each review question (see Appendix D of the full version of the original guideline document). These formed the starting point for systematic reviews of relevant evidence. Published evidence was identified by applying systematic search strategies (see Appendix E of the full version of the original guideline document) to the following databases: Medline (1950 onwards), Embase (1980 onwards), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 onwards) and three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects). Searches to identify economic studies were undertaken using the above databases, the NHS Economic Evaluation Database (NHS EED) and the Health Technology Assessment (HTA) database.

Four of the 14 searches were limited by date appropriate to the interventions being considered (questions relating to biochemical and ultrasound diagnosis of miscarriage, effectiveness of early pregnancy assessment units and treatment setting for management of miscarriage – see protocols in Appendix D of the full version of the original guideline document for details). The searches were limited by language of publication (publications in languages other than English were not reviewed). Generic and specially developed search filters were used to identify particular study designs, such as randomised controlled trials (RCTs). There was no systematic attempt to search grey literature (conference abstracts, theses or unpublished trials), nor was hand searching of journals not indexed on the databases undertaken.

For four of the review topics a joint search strategy was developed and run to cover more than one question within that topic. The databases of identified titles and abstracts were then 'weeded' and papers allocated to their individual question before further weeding. This was carried out for the two ultrasound reviews, the four reviews on human chorionic gonadotrophin and progesterone for diagnosing early pregnancy loss, three reviews on the management of miscarriage (expectant compared with active management, medical compared with surgical management, and dose of mifepristone and misoprostol) and two reviews on anti-D rhesus prophylaxis. Following weeding within each individual question full text versions of remaining studies were ordered. Each full text version was then assessed for inclusion/exclusion against pre-defined criteria as detailed in the protocol. Flow diagrams detailing these processes for each question can be found in Appendix F and details of excluded studies in Appendix G of the full version of the original guideline document.

Towards the end of the guideline development process, the searches were updated and re-executed to include evidence published and indexed in the databases by February 8, 2012.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development, and Evaluation (GRADE)*

Level	Description
High	Further research is very unlikely to change the confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

*The GRADE system described above covers studies of treatment effectiveness. However, it is less well established for studies reporting accuracy of diagnostic tests. For such studies, National Institute for Health and Clinical Excellence (NICE) recommends using the Quality Assessment of Studies of Diagnostic Accuracy (QUADAS) methodology checklist to assess study quality (see the "Availability of Companion Documents" for the NICE guidelines manual, 2009).

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Women's and Children's Health (NCC-WCH), on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Reviewing and Synthesising Evidence

Evidence relating clinical effectiveness was reviewed and synthesised according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach . In the GRADE approach, the quality of the evidence identified for each outcome listed in the review protocol is assessed according to the factors listed below, and an overall quality rating (high, moderate, low or very low) is assigned by combining the ratings for the individual factors.

- Study design (as an indicator of intrinsic bias; this determines the initial quality rating).
- Limitations in the design or execution of the study including concealment of allocation, blinding, loss to follow up (these can reduce the quality rating).
- Inconsistency of effects across studies: occurs when there is variability in the treatment effect demonstrated across studies (heterogeneity) (this can reduce the quality rating).

- Indirectness: the extent to which the available evidence fails to address the specific review question (this can reduce the quality rating).
- Imprecision: present when there is uncertainty around the estimate of effect, for example when the confidence intervals are wide or the sample size or event rate is low (this can reduce the quality rating).
- Other considerations including large magnitude of effect, evidence of a dose-response relationship, or confounding variables likely to have reduced the magnitude of an effect (these can increase the quality rating in observational studies, provided no downgrading for other features has occurred).

The type of review question determines the highest level of evidence that may be sought. For issues of therapy or treatment, the highest possible evidence level is a well-conducted systematic review or meta-analysis of randomised controlled trials (RCTs), or an individual RCT. In the GRADE approach, a body of evidence based entirely on such studies has an initial quality rating of high, and this may be downgraded to moderate, low or very low if factors listed above are not addressed adequately. For issues of prognosis, the highest possible level of evidence is a controlled observational study (a cohort study or case–control study), and a body of evidence based on such studies would have an initial quality rating of low, which might be downgraded to very low or upgraded to moderate or high, depending on the factors listed above.

For each review question the highest available level of evidence was sought. Where appropriate, for example, if a systematic review of RCTs or individual RCTs were identified to answer a question directly, studies of a weaker design were not considered. Where systematic reviews of RCTs or RCTs were not identified, other appropriate experimental or observational studies were sought. For the priority outcome of women's experience of care and psychological outcomes, qualitative studies were sought where appropriate. For diagnostic tests, test evaluation studies examining the performance of the test were used if the accuracy of the test was required, but where an evaluation of the effectiveness of the test in the clinical management of the condition was required, evidence from RCTs or cohort studies was optimal. For studies evaluating the accuracy of a diagnostic test, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios for positive and negative test results (LR+ and LR–, respectively) were calculated or quoted where possible (see Table 3.1 of the full version of the original guideline document).

The GRADE system described above covers studies of treatment effectiveness. However, it is less well established for studies reporting accuracy of diagnostic tests. For such studies, NICE recommends using the Quality Assessment of Studies of Diagnostic Accuracy (QUADAS) methodology checklist to assess study quality (see the NICE guidelines manual, 2009 in the "Availability of Companion Documents").

Some studies were excluded from the guideline reviews after obtaining copies of the corresponding publications because they did not meet inclusion criteria specified by the GDG (see Appendix G of the full version of the original guideline document). The characteristics of each included study were summarised in evidence tables for each review question (see Appendix H of the full version of the original guideline document). Where possible, dichotomous outcomes were presented as risk ratios (RRs) or odds ratios (ORs) with 95% confidence intervals (CIs), and continuous outcomes were presented as mean differences with 95% CIs or standard deviations (SDs).

The body of evidence identified for each review question (or part of a review question) was presented in the form of a GRADE evidence profile summarising the quality of the evidence and the findings (pooled relative and absolute effect sizes and associated CIs). Summary GRADE tables have been reported in the main text, with the full GRADE evidence profiles reported in Appendix I of the full version of the original guideline document. Where possible, the body of evidence corresponding to each outcome specified in the review protocol was subjected to quantitative meta-analysis. In such cases, pooled effect sizes were presented as pooled RRs, pooled ORs or weighted mean differences. By default, meta-analyses were conducted by fitting fixed effects models, but where statistically significant heterogeneity was identified random effects models were used. Where quantitative meta-analysis could not be undertaken (for example because of heterogeneity in the included studies or where studies were not RCTs) the range of effect sizes reported in the included studies was presented.

Incorporating Health Economics

The aims of the health economic input to the guideline were to inform the Guideline Development Group (GDG) of potential economic issues relating to ectopic pregnancy and miscarriage, and to ensure that recommendations represented a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of quality adjusted life years [QALYs]), harms and costs of different care options.

The GDG prioritised a number of review questions where it was thought that economic considerations would be particularly important in formulating recommendations. Systematic searches for published economic evidence were undertaken for these questions. For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using a quality assessment checklist based on good practice in economic evaluation. Reviews of the (very limited) relevant published health economic literature are presented alongside the clinical effectiveness reviews.

Health economic considerations were aided by original economic analysis undertaken as part of the development process. For this guideline the

areas prioritised for economic analysis were:

- Expectant compared with active management of miscarriage
- Management of ectopic pregnancy
- Progesterone for treatment of threatened miscarriage
- Effectiveness of early pregnancy assessment units (EPAUs)

Due to a lack of relevant health economic literature and absence of clinical effectiveness data, it was not possible to undertake economic analysis to determine the cost effectiveness of EPAUs.

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Women's and Children's Health (NCC-WCH), on behalf of the National Institute for Health and Clinical Excellence (NICE). (See the "Availability of Companion Documents" field for the full version of this guidance.)

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Evidence to Recommendations

For each review question recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, the technical team drafted and the Guideline Development Group (GDG) agreed to short clinical and, where appropriate, cost effectiveness evidence statements which were presented alongside the evidence profiles. Statements summarising the GDG's interpretation of the evidence and any extrapolation from the evidence used to form recommendations were also prepared to ensure transparency in the decision-making process. The criteria used in moving from evidence to recommendations were:

- Relative value placed on the outcomes considered
- Consideration of the clinical benefits and harms
- Consideration of net health benefits and resource use
- Quality of the evidence
- Information giving and psychological support
- Other considerations (including equalities issues)

In areas where no substantial clinical research evidence was identified, the GDG members considered other evidence-based guidelines and consensus statements or used their collective experience to identify good practice. The health economics justification in areas of the guideline where the use of National Health Service (NHS) resources (interventions) was considered was based on GDG consensus in relation to the likely cost effectiveness implications of the recommendations. The GDG also identified areas where evidence to answer review questions was lacking and used this information to formulate recommendations for future research.

Towards the end of the guideline development process formal consensus methods were used to consider all the clinical care recommendations and research recommendations that had been drafted previously. The GDG identified 10 "key priorities for implementation" (key recommendations) and five high-priority research recommendations. The key priorities for implementation were those recommendations thought likely to have the biggest impact on the care of women with early pregnancy complications and outcomes in the NHS as a whole: these were selected using two rounds of anonymous voting among the GDG members. In the first round of voting each member was asked to cast 10 votes and the five recommendations that received six or more votes were promoted to become key priorities for implementation. A second round of voting was carried out for all recommendations that received between three and five votes in the first round. Each GDG member was asked to cast five votes. A further three recommendations received six or more votes in the second round and were added to the list of key priority recommendations.

Following consultation with stakeholders, two further recommendations were identified as being key priorities for implementation. The priority research recommendations were selected in a similar way, with one round of voting leading to selection of five key priority recommendations for research.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions that must (or must not) be used
The Guideline Development Group (GDG) usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a 'strong' recommendation
The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when it is confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GDG uses similar forms of words (for example, 'Do not offer…') when it is confident that an intervention will not be of benefit for most patients.

Interventions that could be used
The GDG use 'consider' when it is confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

Health Economics

The aims of the health economic input to the guideline were to inform the Guideline Development Group (GDG) of potential economic issues relating to pain and bleeding in early pregnancy and to ensure that its recommendations represented a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits or harms (ideally in terms of quality adjusted life years [QALYs]) and costs of different care options.

The GDG prioritised the clinical questions where it was thought that economic considerations would be particularly important in formulating recommendations. For this guideline the areas prioritised for economic analysis were:

- Progesterone for threatened miscarriage (see Section 7.2 for summary and Section 10.2 for full details in full version of original guideline document)
- Management of miscarriage (see Section 7.3 for summary and Section 10.3 for full details in full version of original guideline document)
- Management of ectopic pregnancy (see Section 8.2 for summary and Section 10.4 for full details in full version of original guideline document).

See also Section 5.2 for discussion of *Clinical and Cost Effectiveness of Early Pregnancy Assessment Units* (EPAUs) in the full version of the original guideline document.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was validated through two consultations.

1. The first draft of the guideline (the full guideline, National Institute for Health and Clinical Excellence [NICE] guideline, and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Improved diagnosis and initial management of ectopic pregnancy and miscarriage in early pregnancy
- Findings from the descriptive evidence suggest that for some women a follow-up appointment is perceived as valuable, particularly the provision of an opportunity to discuss possible reasons for the pregnancy loss and to help in planning for the future.

Potential Harms

- The provision of additional counselling sessions or other emotional support for women with pain and bleeding in early pregnancy and/or women who experience early pregnancy loss appears not to bestow any clinical benefits as measured by anxiety and depression scales (indeed, some women reported negative experiences following counselling sessions as it involved re-living the experience).
- Women having expectant management of miscarriage had more days of bleeding and a significantly greater chance of needing a blood transfusion. Unplanned intervention was significantly greater in the expectant management group.
- Women undergoing medical treatment required a longer period of recovery and follow-up than women who had laparoscopic surgery. Given the potential risks if medical management fails, the group highlighted the importance of the follow-up protocol, and decided that if any difficulties in follow-up were anticipated, women should be advised to have surgery as a first-line treatment.
- For women with factors prognostic of infertility, the evidence suggested that salpingotomy was associated with a higher chance of a subsequent intrauterine pregnancy.

Contraindications

Contraindications

- Some women may have contraindications to surgery or have a personal desire to avoid a surgical procedure; therefore medical treatment would be appropriate in such circumstances.
- There might be occasions when transabdominal ultrasound would be the better option, such as when women have an enlarged uterus or other pelvic pathology.
- Women may chose laparoscopic salpingectomy if methotrexate is contraindicated.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision.
- Treatment and care should take into account women's needs and preferences. Women should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If women do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent and the code of practice that accompanies the Mental Capacity Act. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.
- If the person is under 16, healthcare professionals should follow the guidelines in the Department of Health's Seeking consent: working with children.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the NICE Web site (http://guidance.nice.org.uk/CG154 ; see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Support and Information Giving

Throughout a woman's care, give her and (with agreement) her partner specific evidence based information in a variety of formats. This should include (as appropriate):

- When and how to seek help if existing symptoms worsen or new symptoms develop, including a 24-hour contact telephone number.
- What to expect during the time she is waiting for an ultrasound scan.
- What to expect during the course of her care (including expectant management), such as the potential length and extent of pain and/or bleeding, and possible side effects. This information should be tailored to the care she receives.
- Information about post-operative care (for women undergoing surgery).
- What to expect during the recovery period – for example, when it is possible to resume sexual activity and/or try to conceive again, and what to do if she becomes pregnant again. This information should be tailored to the care she receives.
- Information about the likely impact of her treatment on future fertility.
- Where to access support and counselling services, including leaflets, web addresses and helpline numbers for support organisations.

Ensure that sufficient time is available to discuss these issues with women during the course of their care and arrange an additional appointment if more time is needed.

Early Pregnancy Assessment Services

Regional services should be organised so that an early pregnancy assessment service is available 7 days a week for women with early pregnancy complications, where scanning can be carried out and decisions about management made.

Symptoms and Signs of Ectopic Pregnancy and Initial Assessment

- During clinical assessment of women of reproductive age, be aware that:
  - They may be pregnant, and think about offering a pregnancy test even when symptoms are non-specific and
  - The symptoms and signs of ectopic pregnancy can resemble the common symptoms and signs of other conditions – for example, gastrointestinal conditions or urinary tract infection.
- All healthcare professionals involved in the care of women of reproductive age should have access to pregnancy tests.

Using Ultrasound for Diagnosis

Offer women who attend an early pregnancy assessment service (or out-of-hours gynaecology service if the early pregnancy assessment service is not available) a transvaginal ultrasound scan to identify the location of the pregnancy and whether there is a fetal pole and heartbeat.

Human Chorionic Gonadotrophin Measurements in Women with Pregnancy of Unknown Location

Be aware that women with a pregnancy of unknown location could have an ectopic pregnancy until the location is determined.

Expectant Management

Use expectant management for 7–14 days as the first-line management strategy for women with a confirmed diagnosis of miscarriage. Explore management options other than expectant management if:

- The woman is at increased risk of haemorrhage (for example, she is in the late first trimester) or
- She has previous adverse and/or traumatic experience associated with pregnancy (for example, stillbirth, miscarriage or antepartum haemorrhage) or
- She is at increased risk from the effects of haemorrhage (for example, if she has coagulopathies or is unable to have a blood transfusion) or
- There is evidence of infection

Surgical Management

Where clinically appropriate, offer women undergoing a miscarriage a choice of:

- Manual vacuum aspiration under local anaesthetic in an outpatient or clinic setting or
- Surgical management in a theatre under general anaesthetic

Performing Laparoscopy

When surgical treatment is indicated for women with an ectopic pregnancy, it should be performed laparoscopically whenever possible, taking into account the condition of the woman and the complexity of the surgical procedure.

Salpingectomy and Salpingotomy

Offer a salpingectomy to women undergoing surgery for an ectopic pregnancy unless they have other risk factors for infertility.

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Patient Resources

Resources

Slide Presentation

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Women's and Children's Health. Ectopic pregnancy and miscarriage. Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Dec. 38 p. (Clinical guideline; no. 154).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Dec

Guideline Developer(s)

National Guideline Alliance - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

All Guideline Development Group (GDG) members' interests were recorded on declaration forms provided by National Institute for Health and Clinical Excellence (NICE). The form covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry. GDG members' interests are listed in this section. Except where specifically indicated in the table, these interests did not constitute a conflict.

The GDG members' declarations of interests are listed in Appendix C in the full version of the guideline (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Ectopic pregnancy and miscarriage. Full guideline. London (UK): National Institute for Clinical Excellence (NICE); 2012 Dec. 287 p. (Clinical guideline; no. 154). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .
- Ectopic pregnancy and miscarriage. Appendices. London (UK): National Institute for Clinical Excellence (NICE); 2012 Dec. 531 p. (Clinical guideline; no. 154). Electronic copies: Available in PDF from the NICE Web site .
- Ectopic pregnancy and miscarriage. Evidence tables. London (UK): National Institute for Clinical Excellence (NICE); 2012 Dec. 628 p. (Clinical guideline; no. 154). Electronic copies: Available in PDF from the NICE Web site .
- Ectopic pregnancy and miscarriage. Baseline assessment tool. National Institute for Health and Clinical Excellence (NICE); 2012. (Clinical guideline; no. 154). Electronic copies: Available from the NICE Web site .
- Ectopic pregnancy and miscarriage. Clinical audit tools. National Institute for Health and Clinical Excellence (NICE); 2012 Dec Various p. (Clinical guideline; no. 154). Electronic copies: Available from the NICE Web site .
- Ectopic pregnancy and miscarriage. Electronic audit tools. National Institute for Health and Clinical Excellence (NICE); 2012 Dec. (Clinical guideline; no. 154). Electronic copies: Available from the NICE Web site .
- Ectopic pregnancy and miscarriage: clinical case scenarios. National Institute for Health and Clinical Excellence (NICE); 2012 Dec. (Clinical guideline; no. 154). Electronic copies: Available in PDF and PowerPoint from the NICE Web site .
- Ectopic pregnancy and miscarriage. Costing report. National Institute for Health and Clinical Excellence (NICE); 2012 Dec. 39 p. (Clinical guideline; no. 154). Electronic copies: Available in PDF from the NICE Web site .
- Ectopic pregnancy and miscarriage. Costing template. National Institute for Health and Clinical Excellence (NICE); 2012 Dec. (Clinical guideline; no. 154). Electronic copies: Available from the NICE Web site .
- Ectopic pregnancy and miscarriage. Podcast. National Institute for Health and Clinical Excellence (NICE); 2012. (Clinical guideline; no. 154). Electronic copies: Available from the NICE Web site .
- NICE Pathways. Ectopic pregnancy and miscarriage: Overview. London (UK): National Institute for Clinical Excellence (NICE); 2012 Dec. Electronic copies: Available from the NICE Web site .

- The guidelines manual 2009. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Jan. Electronic copies: Available in Portable Document Format (PDF) from the NICE Archive Web site .

Patient Resources

The following is available:

- Ectopic pregnancy and miscarriage in early pregnancy. Information for the public. London: National Institute for Health and Clinical Excellence (NICE); 2012 Dec. Electronic copies: Available in from the National Institute for Health and Clinical Excellence (NICE) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI Institute on March 12, 2013.

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